UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,150	11/19/2001	Dario Cremaschi	216261US0CONT	8275

22850 7590 11/07/2003

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/988,150	CREMASCHI ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 11-28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 11-28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11-19-01 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 11-28 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13, 15-22, and 24-28, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of intranasally administering a composition comprising a microparticle having a protein and an antibody adsorbed thereon, wherein said administering comprises contacting a microparticle having a protein and an antibody thereon with the nasal mucosa of a patient in need thereof and wherein said antibody is specific for the protein, does not reasonably provide enablement for the broadly claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are broadly drawn to a method for intranasally administering a composition comprising a microparticle that has a protein and an antibody adsorbed theron. Hence, the claims broadly include a composition that contains any and all proteins combined with any and all antibodies on a microparticle.

However, one cannot extrapolate the teachings of the specification to the scope of the claims because it is not clear how one of skill in the art would know how to predictably use the invention as claimed with any and all polypeptides that further may comprise non-specific antibodies. The specification teaches (page 6) that the antibody is "preferably specific for the protein" and it not clear how an antibody adsorbed to a microparticle would bind to any and all proteins. For example, how would insulin be received by a patient if it is not bound to an anti-insulin antibody on the microparticle? Thus, it does not seem reasonable that the claimed composition would successfully pass through the nasal lymphatics of a patient if the adsorbed antibodies are not specific for the particular protein.

Therefore, in view of the breadth of the claims, and reasoning set forth above, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-28 are rejected under 35 USC 103(a) as being unpatentable over Smith *et al.* (WO94/28879, IDS) in view of Almeida *et al.* ("Nasal Delivery of Vaccines", Jnl. of Drug Targeting, 1996, Vol. 3, pages 455-467)

The claims are drawn to a method for intranasally administering a composition comprising a microparticle having a protein and an antibody adsorbed thereon, wherein said administering comprises contacting a microparticle having a protein and an antibody thereon with the nasal mucosa of a patient in need thereof (Claim 11) or a method for intranasally administering a composition comprising a microparticle and an antibody adsorbed thereon, wherein said administering comprises having a protein and an antibody thereon with the nasal mucosa of a patient in need thereof, and wherein the transepithelial transport obtained with 3.2 x 10^{11} microparticles/ml is 1.7 $^{0}/_{00}$ (Claim 20).

Claims 11 and 20 are further limited to wherein said protein is selected from the group consisting of BSA, insulin, enkephalin, hormones, growth factors, cytokines, coagulation factors, polypeptides, and antimicrobial agents (Claims 12, 21); wherein said antibody is an immunoglobulin selected from the group consisting of IgM, IgA, and IgG (Claims 13, 22); wherein said immunoglobulin is specific for the protein (Claims 14, 23); wherein said microparticle is biodegradable (Claims 15, 24); wherein said microparticle comprises

polystyrene (Claims 16, 25); wherein the ratio of protein to antibody is 1 to 15, 000 (Claims 17, 26), 1 to 5000 (Claims 18, 27), or 1 to 100 (Claims 19,28) moles of protein per mole of antibody.

1. Smith teaches a method for administering a composition comprising a microparticle having a protein and an antibody adsorbed thereon, wherein said administering comprises contacting a microparticle having a protein and an antibody thereon for **oral** administration (see abstract); wherein said protein is selected from the group consisting of BSA, insulin, enkephalin, hormones, growth factors, cytokines, coagulation factors, polypeptides, and antimicrobial agents (see page 6); wherein said antibody is an immunoglobulin selected from the group consisting of IgM, IgA, and IgG (see page 3); wherein said immunoglobulin is specific for the protein (see page 4) wherein said microparticle is biodegradable (see page 7); wherein said microparticle comprises polystyrene (see page 8); wherein the ratio of protein to antibody is 1 to 15, 000, 1 to 5000, or 1 to 100 moles of protein per mole of antibody (see page 19). Smith further teaches the presence of M cells along the epithelial lining of the intestine which are more easily penetrated by macromolecules (page 2, lines 19-32) and that the presence of M cells is advantageous because the peptide or protein will pass into the lymphatic system rather than into the blood and this may mean that bioavailability is increased because hepatic first pass metabolism will be avoided.

2. Smith *et al.* do not teach a method of *intranasal* administration of the above composition nor does Smith explicitly teach that transepithelial transport obtained with 3.2×10^{11} microparticles/ml is $1.7\ ^{0}/_{00}$.

3. Almeida *et al* summarize the current state of the art and the advantages of nasal delivered medicines. Among the advantages offered by this route are the valuable mucosal surface of approximately 150 cm^2, the accessibility and easy administration that increases patient compliance, and a highly vascularized and venous flow that escapes the portal system, thus preventing first-pass metabolism in the liver (page 457). Almeida *et al.* further teach that nasal inoculation involves the uptake of particulate antigens mainly by the M cells of the lymphoid tissue (page 458).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include nasal administration of the claimed composition as taught by Smith *et al.* because Almeida *et al.* teach the advantages of nasal delivered medicines including, the accessibility and easy administration that increases patient compliance, and a highly vascularized and venous flow that escapes the portal system, thus preventing first-pass metabolism in the liver (page 457). One would have been motivated to do so because both Smith *et al.* and Almeida *et al.* attribute the bioavailability via either route to the presence of M-cells, either in the epithelial lining of the intestine or in the nasal mucosa. Furthermore, although the Almeida *et al.* reference does not characterize that a transepithelial transport ratio of 1.7 $^0/_{00}$ is obtained with 3.2 x 10^{11} microparticles/ml, one of ordinary skill would have a reasonable expectation that such a yield is achieved due to the valuable mucosal surface of approximately 150 cm^2 as reported by Almeida *et al.*

No claim is allowed.

The following prior art is provided and made of record (although not relied upon) is considered pertinent to applicant's disclosure:

Smith *et al.* Experimental Physiology, 1995, Vol. 80, pages 735-743.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
November 5, 2003

Gary B Nickol